

Application No. 10/668,214
Reply to Office Action of November 4, 2005

IN THE CLAIMS

Please amend the claims as follows:

Claims 1-65 (Cancelled).

Claim 66 (Previously Presented): A method of providing a therapeutic benefit to a patient comprising:

culturing mature human cells which are differentiated to a point where they are programmed to develop into a specific type of cell tissue in a liquid culture medium which is replaced at a rate of at least 25% daily replacement continuously for more than one day and for a time sufficient to obtain mature human cells ~~lineage committed~~ with enhanced biological function, which is relative to the biological function of the human cells that are cultured in static culture; and

transferring said cultured cells into said patient.

Claim 67 (Previously Presented): The method of claim 66, wherein the culture medium is continuously perfused at a ramped rate proportional to the lactate concentration and/or cell density to replace the culture medium without substantial dilution of the cell density.

Claim 68 (Previously Presented): The method of claim 66, wherein replacement of said medium comprises perfusing fresh medium through at least part of the mass of said human cells.

Claim 69 (Previously Presented): The method of claim 66, wherein said medium comprises animal or human sera or plasma.

Claim 70 (Previously Presented): The method of claim 66, comprising maintaining glucose concentration in said medium in the range of from 5 to 20 mM, lactate concentration

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in said medium below about 35 mM, glutamine concentration in said medium in the range of from 1 to 3 mM, and ammonia concentration in said medium below 2.4 mM.

Claim 71 (Previously Presented): The method of claim 66, further comprising removing nonadherent cells continuously, periodically, or intermittently, without disturbing adherent cells.

Claim 72 (Cancelled).

Claim 73 (Previously Presented): The method of Claim 66, wherein said human cells are selected from the group consisting of hepatocytes, neural cells, epithelial cells, keratinocytes, endothelial cells and mesenchymal cells.

Claim 74 (Previously Presented): The method of Claim 73, wherein said human lineage committed tissue cells are mesenchymal cells.

Claim 75 (Currently Amended): The method of Claim 74, wherein said mesenchymal cells are selected from the group consisting of chondrocytes, osteoblasts, myeoblasts, fibroblasts, tenoblasts, ~~bone marrow stromal cells~~, tenocytes, adipocytes, osteocytes, and myocytes.

Claim 76 (Cancelled).

Claim 77 (Previously Presented): The method of Claim 66, wherein the liquid medium is replaced at a rate equal to 50 to 100% daily replacement for a cell density of from 1×10^4 to 1×10^7 cells per ml of culture.

Claim 78 (Previously Presented): The method of claim 77, wherein said medium comprises animal human sera or plasma.

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Claim 79 (Previously Presented): The method of claim 77, comprising maintaining glucose concentration in said medium in the range of from 5 to 20 mM, lactate concentration in said medium below about 35 mM, glutamine concentration in said medium in the range of from 1 to 3 mM, and ammonia concentration in said medium below 2.4 mM.

Claim 80 (Previously Presented): The method of claim 77, further comprising removing nonadherent cells continuously, periodically, or intermittently, without disturbing adherent cells.

Claim 81 (Previously Presented): The method of Claim 77, wherein said human lineage committed tissue cells are selected from the group consisting of hepatocytes, neural cells, epithelial cells, keratinocytes, endothelial cells and mesenchymal cells.

Claim 82 (Previously Presented): The method of Claim 81, wherein said human lineage committed tissue cells are mesenchymal cells.

Claim 83 (Currently Amended): The method of Claim 82, wherein said mesenchymal cells are selected from the group consisting of chondrocytes, osteoblasts, myeoblasts, fibroblasts, tenoblasts, bone marrow stromal cells, tenocytes, adipocytes, osteocytes, and myocytes.

Claim 84 (Withdrawn): The method of Claim 76, wherein the human cells are cultured for at least 2 days.

Claim 85 (Previously Presented): The method of Claim 76, wherein the culture medium contains at least 1 growth factor which stimulates the proliferation of the cells.

Claim 86 (Withdrawn): The method of Claim 66, wherein the therapeutic benefit provided to the patient is generation of a tissue.